PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70) 10/552095

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
10/668/PWO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/001464	02.04.2004	04.04.2003

International Patent Classification (IPC) or national classification and IPC
A61L15/22, A61L15/32, A61L24/10, A61L24/04, A61L26/00, A61L31/04

Applicant
TISSUEMED LIMITED et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.01.2005	08.07.2005

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/001464

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-40	as originally filed
Claims, Numbers	
1-62	as originally filed
Drawings, Sheets	
1/3-3/3	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/GB2004/001464

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 53-62

because:

☒ the said international application, or the said claims Nos. 53-62 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/001464

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-52
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1-52
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1-52
	No:	Claims	-

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Since claims 53-62 are directed to a method of treatment of the human or animal body by surgery/therapy, they relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. For the assessment of the subject-matter of present claims 53-62 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States.
Therefore, no opinion will be formulated with respect to the subject-matter of claims 53-62 (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents (D1 and D2) cited in the International search report:

D1 ... WO 02/34304 A (Tissuemed Limited)
D2 ... DE 198 59 611 A (Centeon Pharma GmbH)

Document D1 discloses (cf. page 1, line 9 - page 2, line 13) a self-adhesive, hydratable polymer matrix in form of a sheet, patch, or film for the application to internal and external body surfaces. The matrix comprises a polymerisable and/or crosslinkable material that supports wound healing and a synthetic polymer having bioadhesive properties enabling the matrix to adhere to underlying tissue by means of ionic and/or hydrogen bonding.

Document D2 discloses (cf. page 1, lines 20-59 ; claims 1-4, 7, 8) a fibrin adhesive containing thrombin, fibrinogen, factor XIII and a calcium salt in granulate form with a particle size of 50 µm to 1000 µm.

The subject-matter of claims 1-52 of the present application differs from D1 and D2 in the

presence of tissue-reactive functional groups and is therefore novel according to Article 33(2) PCT.

Document D1, which is considered the most relevant state of the art, discloses (cf. page 1, line 9 - page 2, line 13) a self-adhesive, hydratable polymer matrix in form of a sheet, patch, or film for the application to internal and external body surfaces to provide a tissue adhesive which does not require manipulation *in situ* using mechanical attachment or external activation.

The objective technical problem underlying the present application is considered to improve the adhesion strength of the tissue adhesive in D1.

The solution proposed in claim 1 of the present application is a particulate polymerisable and/or crosslinkable material in particulate form, the material being in admixture with particulate material comprising tissue-reactive functional groups.

The difference between the subject-matter of claims 1, 45 and 52 of the present application and D1 is a) the particulate form of the two materials and b) the presence of tissue-reactive functional groups in the second material.

According to the description of the present application (cf. p. 3, l. 21-32), the particulate formulation has the advantage to be easy to apply and to adhere to the tissue by van der Waals and/or hydrogen bonding. On contact with the tissue surface, the formulation becomes hydrated and reaction between the tissue-reactive functional groups and the underlying tissue surface takes place, resulting in high adhesion of the matrix to the body tissue.

Since the skilled person had no indication to use a material comprising tissue-reactive functional groups in the tissue-adhesive formulation and the bonding strength of the claimed tissue adhesive is clearly improved due to the chemical bonding, the subject-matter of claims 1-52 is considered to involve an inventive step according to Article 33(3) PCT.